Allergy Abstracts

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Asthma and Hay Fever

Irradiation of the Nasopharynx in Children With Infectious Asthma. Mueller, H. L., and Flake, C. G.: New England J. Med. **246**: 924, 1952.

Forty-one asthmatic children were chosen for irradiation therapy of the nasopharynx. The following criteria were used in the selection of patients: a history of severe asthma for over two years associated with respiratory infections; failure to achieve satisfactory results with other methods of therapy for infectious asthma; control of associated asthma due to other allergens by allergic management and treatment; and the presence of hypertrophied lymphoid tissue in the nasopharynx, or evidence of infection, or both. The patients were graded according to the severity of the asthma. Part of the group was treated with one or two series of applications of radium in a standard applicator to the nasopharynx. The remaining children were treated with one or two series of x-ray irradiation treatments to the nasopharynx. Twenty-four patients had had a tonsillectomy and adenoidectomy at least one year prior to the treatment. There was no significant difference in the results of treatment with radium application or with x-ray irradiation. Eleven of the 41 patients obtained complete relief from asthma for periods of from two to four years. Excellent results were obtained in 17 patients for periods of eighteen months to four years. Five cases obtained only fair results. Eight patients, all with severe asthma, experienced unsatisfactory results. It is suggested that the good results obtained were due to the elimination of foci of chronic or recurring infections. The authors conclude that irradiation therapy is a valuable and effective treatment in selected cases of infectious asthma in children. B. S.

Ambulant Treatment of Bronchial Asthma With Corticotropin. Andersson, E.: Ugesk. f. læger. **114**: 1284, 1952.

Thirteen patients with severe bronchial asthma, who had not responded to the usual forms of therapy, were treated on an ambulatory basis with corticotropin for six days. Fifty milligrams were injected twice daily for the first two days and 30 mg. twice daily for the other four days. Subjective symptoms disappeared in 11 patients. Improvement began from twenty-four to forty-eight hours after the first injection. Remissions lasted from one to sixty-seven days. The author advises that corticotropin be used only in severe cases after other therapy has failed. H.

Visammin in Treatment of Bronchial Asthma. Merli, A., and Mariani, R.: Minerva med. **43**: 400, 1952.

Visammin has a strong antispasmodic action, relaxes the bronchial musculature, increases the vital capacity, and dilates the coronary arteries. These effects are always proportional to the dose administered. Visammin was administered orally and rectally to 19 hospitalized patients, 6 of whom had bronchial asthma and 13 of whom had chronic asthmatic bronchitis. The initial daily dose varied from 100 to 300 mg. The average daily maintenance dose was either 50 or 100 mg. The drug was well tolerated by all patients. Satisfactory results were obtained in 13 patients. H.

Changes in the Serum Calcium and Potassium Values of Bronchial Asthmatics After Extirpation of the Carotid Body. Suzuki, T.: Tohoku J. Exper. Med. **40**: 57, 1950.

Serum calcium values were found to be normal in 87 patients with bronchial asthma. The values for serum potassium were above normal in 41 per cent of this group. Extirpation of the carotid body resulted in a sudden increase of serum calcium and a sudden decrease of potassium. H.

Asthma From Ricinus. Bassi, D., and Berto, R.: Policlinico (sez. prat.) **58**: 417, 1951.

The authors review a large number of cases of allergy to ricinus (Castor bean) seeds. Bronchial asthma was frequently observed in the regions where these seeds were grown. Positive cutaneous and passive transfer reactions were obtained in a number of cases. H.

Dermatology

A Study of Eczematous Sensitivity to Formaldehyde. Rostenberg, A., Jr., Bairstow, B., and Luther, T. W.: J. Investigation Dermat. **19**: 459, 1952.

Five nurses who had developed a contact dermatitis to formaldehyde following the handling of thermometers immersed in 10 per cent formaldehyde solution were studied. All had positive reactions to patch tests with a 1:20 formalin solution. Positive reactions were not obtained in dilutions weaker than 1:200. Patch tests with acetaldehyde, benzaldehyde, formic acid, and paraldehyde gave negative reactions. For some unexplainable reason, 4 of the patients reacted to the aldehyde in oil of cinnamon. Intracutaneous testing with formalized protein (formaldehyde and human serum albumin) and with formaldehyde in dilutions of from 1:2,500 to 1:7,500 often produced delayed reactions. Because the formalized protein contained some free formal-

dehyde (a dilution of about 1:5,000), it is possible that the free formaldehyde may have been responsible for these delayed reactions. Since several of the patients showed no reactions to patch tests during the first twenty-four or forty-eight hours, the importance of examining all reactions for at least seventy-two hours is stressed. Due to its sensitizing properties, formaldehyde should not be used for storing thermometers. R. W.

Effects of Simultaneous Skin Tests on Size of Tuberculin Reactions. Crumb, C., Meier, P., and Siebert, F. B.: Am. Rev. Tuberc. **65**: 201, 1952.

Guinea pigs previously injected with a moderately virulent strain of human-type tubercle bacillus were skin tested with a number of tuberculin products. These included the standard product, PPD-S, a purified whole protein fraction isolated from heated tuberculin; an A-type protein fraction, known to be more potent than the standard; and a C-protein fraction, much less potent than the standard. These latter fractions were isolated from unheated tuberculin filtrates. The guinea pigs were divided into 4 groups of 5 animals each. Groups 1, 2, and 3 each received a single test with a different substance in each of the first three weeks; group 4 was given the 3 substances simultaneously each week for three weeks. In the fourth week, groups 1, 2, and 3 received multiple tests while group 4 received a single test. All tests were given intracutaneously in a dose of 0.0025 mg. per 0.1 ml., based on micro-Kjeldahl nitrogen determinations. There was no evidence of a progressive increase or decrease in sensitivity due to repeated tests with any of the substances. The differences between single and multiple tests with all substances were, on the whole, small. The reactions to one tuberculin fraction (substance C was significantly smaller when given with other substances than when given alone. E. W.

Observations on the Effects of Antihistamine Drugs on the Reactions of the Skin Vessels to Carbaminoyl Choline. Moynahan, E. V.: Brit. J. Dermat. **64**: 1, 1952.

The suppressive effects of antihistaminic drugs on the whealing response of the skin to histamine and carbaminoyl choline were studied. The subjects included 18 healthy volunteers of both sexes ranging in age from 20 to 40 years. Carbaminoyl choline in a dilution of 1:100 and histamine in a dilution of 1:1,000,000 were introduced into the volar surface of the forearms of these subjects by the electrophoretic technique. Studies were made before the oral administration of 100 mg. of Anthisan or 25 mg. of Phenergan and at intervals of two and four hours after these drugs were given. Wheal and flare diameters were measured. An approximately parallel reduction in both wheal and flare reactions from carbaminoyl choline and histamine was noted in 7 subjects. In one subject, results showed a predominantly anticholinergic effect and in another an antihistamine effect. In the remainder of the subjects, no suppressive effects were noted. Since both Phenergan and Anthisan are known to have strong antihistaminic effects and weak anticholinergic effects, it was concluded that the reduction by these drugs of the skin reaction to iontophoretically introduced carbaminoyl choline was due to their effect against histamine. E. W.

Delayed Reactions to Bouillon Medium of Tuberculin. Lichtenstein, M. R., and Cilella, C. A.: Dis. Chest **22**: 163, 1952.

The skin responsiveness to old tuberculin and that to the bouillon media of tuberculin were compared. These studies were conducted in a tuberculosis sanatorium and the subjects tested included 88 student nurses, 150 employees, 34 tuberculous children, 426 tuberculous adults, and 18 tuberculous adults

over 60 years of age. All subjects were tested by the usual Mantoux technique. Reactions were considered negative if there was no induration, doubtful when indurated up to 5 mm., and positive when over 5 mm. in diameter. In a large majority of cases, tests were made with old tuberculin 1:10,000 and bouillon 1:10. Tests with bouillon 1:100 and 1:1,000 were also made. All the tuberculous patients had been tested months previously with old tuberculin. Sixteen patients who were negative to the initial bouillon test in a dilution 1:10 received 10 successive intracutaneous tests at 48-hour intervals. Seventy-four of the affiliate nurses who were completely insensitive to tuberculin in all four strengths, including 10 mg. of old tuberculin and bouillon 1:10, were retested at the end of two months. Positive reactions to bouillon were indistinguishable from the usual tuberculin reaction except that they were of shorter duration. The large majority of positive reactions were obtained with bouillon in the 1:10 dilution. Forty-four per cent of the adult patients and 20 per cent of the tuberculin-positive employees showed positive reactions. Fifty per cent of the tuberculous children and 16 per cent of the adults reacted to bouillon 1:100. Of the 88 affiliate student nurses, 14 were tuberculin-positive. Of these 4 were positive to bouillon 1:10. Of the 74 tuberculin-negative nurses, none was positive to bouillon 1:10. Thirty-four of these nurses who received 12 injections of both tuberculin and bouillon remained negative to both. Of 16 tuberculin-positive, bouillon-negative patients who received 10 successive injections of bouillon 1:10, none remained negative. Of 36 tuberculin-positive employees, 33 per cent responded positively to bouillon 1:10. Eighteen tuberculin-positive employees failed to respond to bouillon. Hence, certain preparations of bouillon media are capable of eliciting positive delayed reactions in a high percentage of tuberculin reactors. Those who were negative on the first test with bouillon could not be sensitized by multiple injections. E. W.

The Use of Corticotrophin (ACTH) and Cortisone in Urticaria and Dermatitis Venenata. Ekblad, G. H.: U. S. Armed Forces M. J. **3**: 839, 1952.

Twenty-eight hospitalized patients with severe acute urticaria, 6 patients with chronic urticaria, and 10 patients with acute dermatitis venenata received one-day courses of ACTH or cortisone. Of the patients with acute urticaria whose disease had lasted from two to forty-two days, 20 were treated with ACTH and all except 2 were markedly improved within thirty-six hours. Six of these patients had relapses which were again treated with ACTH or cortisone. Three of these continued to suffer relapses. Of 16 patients with acute urticaria who received cortisone, 11 had good responses. The subsequent course of the illness in the cortisone-treated patients paralleled that in those treated with ACTH. In general, ACTH was more effective in acute urticaria than cortisone in the doses used. Of 6 patients with chronic urticaria treated with these drugs, one patient experienced improvement which lasted a week. Of 10 patients with severe acute dermatitis venenata treated with ACTH or cortisone, 7 estimated their relief from 50 to 75 per cent. All of the patients experienced some recurrence of symptoms. Despite the relief experienced in dermatitis venenata, no objective evidence of improvement was noted. In 2 patients with atopic dermatitis, 2 with infectious eczematoid dermatitis, and one with deep-seated vesicular or eczematous id reactions, there was no favorable response to this short-term treatment. E. W.

Otorhinology and Ophthalmology

Hydrocortisone (Compound F) in Ophthalmology: Clinical and Experimental Studies. McDonald, P. R., Leopold, I. H., Vogel, A. W., and Mulberger, R. D.: Arch. Ophth. **49**: 400, 1953.

Forty-six patients with a wide variety of ocular diseases were treated with hydrocortisone either in the form of drops or by subconjunctival injection. Twenty-eight of these patients had previously been treated with cortisone locally or systemically. In 18 of the patients, hydrocortisone produced better results than did cortisone. In 4 patients with vernal conjunctivitis, the response to hydrocortisone was dramatic. In no instance was cortisone found to be effective when hydrocortisone was ineffective. Although the spectrum of activity of the two compounds appears to be about the same, hydrocortisone seems to be more potent.

In a series of comparative experiments on rabbit eyes, cortisone (compound E) and hydrocortisone (compound F) were compared dose for dose for their effect on: (1) the permeability of the blood aqueous barrier to fluorescein and streptomycin in the normal and inflamed eye; (2) corneal vascularization induced by intracameral injection of alloxan; and (3) wound healing. The action of both compounds was the same. Neither hormone was found to possess antihistaminic or anticholinergic action. C.

Miscellaneous Allergies

Allergy to Viral and Rickettsial Vaccines. III. Influence of Repeated Inoculations on the Acquisition of Egg Allergy. Ratner, B., Untracht, S., and Hertzmark, F.: New England J. Med. **246**: 533, 1952.

Three hundred nineteen children under treatment for tuberculosis were injected with chick-egg propagated influenza viral vaccine or mumps viral vaccine, or both. Skin tests were done with egg and chicken antigens and with vaccines, before and after the immunizing injections, to determine whether sensitivity had been acquired. Each subject received from 11 to 35 immunizing injections at varying intervals over periods ranging from twelve to twenty-seven months. Thirty-two subjects served as controls and received only skin tests. Five of the 319 immunized cases developed positive skin reactions to egg white, but none of them became clinically sensitive to egg. Another group of 13 children, comprised of cases having a past history of egg sensitivity but now able to tolerate egg and of cases with positive skin reactions to egg but no clinical sensitivity, were injected with influenza virus vaccine diluted 1:10 with saline and combined with a small amount of epinephrine. Generalized reactions were not observed in this group and none developed clinical egg sensitivity during a one-year period of observation. One clinically egg-sensitive child developed a generalized urticarial eruption within thirty minutes after receiving a subcutaneous injection of influenza virus vaccine. When clinically egg-sensitive children were immunized with a refined vaccine (Sharples centrifuged vaccine) by the intracutaneous route, local reactions occurred, but there were no systemic reactions. These children were also able to tolerate this vaccine when given subcutaneously and combined with epinephrine. There was no enhancement of egg sensitivity in these cases. When 120 allergic children, not sensitive to egg, were injected with the vaccine, no clinical or skin sensitivity to egg was noted. It was concluded that the hazard of sensitization from repeated immunizations with viral and rickettsial vaccines is negligible. B. S.

Allergy to Heparin. Midttun, O.: Tidsskr. Norske. Zaegefaren **72**: 241, 1952.

A patient went into a state of collapse lasting for five minutes, immediately following the intracutaneous injection of heparin. Positive reactions were obtained to intracutaneous and passive transfer tests with heparin. A second patient suffering from myocardial infarction developed a prickling

sensation of the skin, generalized erythema, dizziness, and vomiting within five minutes following the injection of heparin. This patient also showed positive intracutaneous and passive transfer reactions to heparin. H.

Allergic Reactions to Cortisone and ACTH. DeSeze, S., Ryckewaert, A., Robin, J., Debeyre, N., and Renier, J. C.: Rev. Rhuma **19**: 608, 1952.

Generalized urticaria was observed in some patients, with no previous history of urticaria, after prolonged cortisone therapy. An unusually high incidence of allergic reactions was noted in patients in whom gold salts were used in conjunction with cortisone. In one case the administration of ACTH provoked the reappearance of an urticaria cleared three days previously by antihistaminics. In one case of gastrointestinal allergy, neither cortisone nor ACTH had any beneficial effect.

The authors suggest that the beneficial effects which result from the administration of ACTH and cortisone for short periods are due to inhibition of certain tissue activities. Prolonged administration of these drugs may cause inhibition of fibroblast formation, interference with antibody formation, and general disturbances of hormone metabolism. H.

The Efficacy of the Intracutaneous Route of Injection and the Susceptibility of the Hartley Strain of Guinea Pigs in Experimental Allergic Encephalitis. Lipton, M. M., and Freund, J.: J. Immunol. **70**: 326, 1953.

Allergic encephalitis was produced regularly in the Hartley strain of guinea pig by a single intracutaneous injection of rabbit spinal cord combined with various adjuvants, such as dried tubercle bacilli, an oil (Bayol F), and an emulsifying agent. Mixed breeds of guinea pigs were less susceptible to this disease than those of the Hartley strain. The intracutaneous route of injection of the allergen was found to be superior to the subcutaneous route in producing this experimental disease. In view of the fact that mice and monkeys require several injections to become sensitized and that rabbits develop encephalitis spontaneously, the authors' method requiring only a single sensitizing injection in the Hartley strain of guinea pigs seems especially suited for quantitative study of allergic encephalitis. M. Cohen.

Anaphylaxis

Skin Reactions in Guinea Pigs Sensitized by Serum Proteins. Winter, L. B.: J. Physiol. **112**: 446, 1951.

Guinea pigs, sensitized intraperitoneally with horse serum, horse serum globulin, or horse serum albumin, were tested on the abdomen from twenty-six to 191 days later by both the scratch and the intracutaneous methods. Results were read three, twenty-four, forty-eight, and seventy-two hours later. Positive reactions to intracutaneous tests were observed in 15 of 78 animals. The reactions consisted of a 3 mm. erythematous area which appeared from two to three hours after the test injection and faded within twenty-four hours. In no instance was a positive reaction obtained by scratch testing.

One week after skin testing, the uterine horns were removed from some animals for in vitro testing and the remaining animals were challenged with intravenous injections of the specific antigen. Most of the animals showed either in vivo or in vitro anaphylactic sensitivity. The incidence of anaphylactic sensitivity was highest in those animals in which the time interval be-

tween the sensitizing and challenging injections was the longest. There was no correlation between the presence of positive skin reactions and positive in vitro reactions. R. W.

Electrocardiographic Studies of the Effect of Histamine on the Cardiac Mechanism. Criep, L. H., and Riley, W. K.: Am. Heart J. **41**: 423, 1951.

Histamine shock was produced in guinea pigs and rabbits while electrocardiographic tracings were being taken. Similar studies were carried out following the administration of Benadryl. The electrocardiographic changes observed are described in detail. The changes which occurred "are identical with those produced by artificial asphyxia through ligation of the trachea" and are also similar to the variations in heart rate, conduction, and alterations in T waves which occur in anaphylactic shock. When sufficient amounts of Benadryl were administered to protect the guinea pig from shock, there was only "slight elevation of the ST segment in Lead I and the left chest lead, with a persistent tachycardia." At one hour, the electrocardiogram was normal. Similar findings were observed in rabbits. K.

Histamine Sensitivity and Anaphylaxis in the Pertussis-Vaccinated Rat. Malkiel, S., and Hargis, B. J.: Proc. Soc. Exper. Biol. & Med. **81**: 689, 1952.

Rats inoculated with *Hemophilus pertussis* were found to lose their insensitivity to histamine. Thirteen of 17 vaccinated animals died within twenty-four hours after histamine was injected intraperitoneally, whereas only 2 of 10 unvaccinated control animals died after similar injections. When *H. pertussis*-vaccinated rats were sensitized with horse serum and challenged with the homologous antigen 94 per cent died. When unvaccinated rats were similarly treated none died. Cortisone administered at appropriate intervals protected the sensitized, vaccinated rat against fatal anaphylactic shock. Pathologic studies were performed on all experimental groups of rats. Pathologic changes were noted only among the vaccinated rats that died in histamine or anaphylactic shock. These consisted of right heart dilatation, collapsed lungs, congestion of the liver and brain. There was marked congestion of the adrenal medulla and minimal cortical congestion. B. S.

The Influence of ACTH and Cortisone Upon Experimental Achorion Quinckeanum Infection and Upon Anaphylaxis in Guinea Pigs. Reiss, F., and Caroline, L.: J. Investigation Dermat. **19**: 365, 1952.

In the first part of the article, the authors describe their studies on the effect of ACTH and cortisone on Achorion Quinckeanum infections. In their anaphylaxis studies, 4 quinea pigs, treated with cortisone for seven consecutive months, were sensitized with horse serum subcutaneously. Three weeks later, they were challenged with an intravenous injection of the antigen. Three animals treated with ACTH for seven consecutive months were similarly sensitized and shocked with horse serum. Two untreated animals were used as controls. Hormone therapy was continued until the day of the challenging injection. All the cortisone-treated animals died in anaphylactic shock. Only 1 of the 3 ACTH-treated animals died in shock. The 2 surviving guinea pigs sustained mild shock symptoms. It is concluded that neither ACTH nor cortisone is capable of preventing the development of anaphylactic sensitivity. R. W.

Pharmacology, Physiology, and Pathology

Further Investigation of Effect of Colloidal Materials Upon the Shwartzman Phenomenon. Bennett, I. L., Jr.: Proc. Soc. Exper. Biol. & Med. **81**: 248, 1952.

Resistance to the Shwartzman reaction was induced in rabbits by repeatedly eliciting the reaction with alternating intracutaneous and intravenous injections of a *Serratia marcescens* filtrate. After at least two negative reactions were obtained, the animals were again prepared for the reaction by an intracutaneous injection of filtrate and, at varying intervals before the provocative intravenous injection twenty-four hours later, one of the colloidal materials under study was injected. The two colloids studied were thorotrast, a suspension of approximately 25 per cent thorium dioxide, and Angiopac, a colloidal organic iodide preparation. The injection of either of these materials immediately following skin preparation or at any time up to thirty minutes prior to the provocative injection of the filtrate abolished the resistance to the Shwartzman phenomenon. It was also found that when animals were pretreated with thorotrast within twenty-four hours before the intracutaneous injection of filtrate, there was a marked increase in the local inflammatory reaction to the bacterial toxin, as compared to the reaction obtained in the controls. Furthermore, when the colloidal materials were injected prior to the provocative intravenous injection of the filtrate, the lethal effect of the bacterial toxin was strikingly enhanced. It is suggested that the colloids exert their effect upon resistance to bacterial toxins by localizing in the macrophages of the reticuloendothelial system and producing a "blockade." B. S.

Effect of ACTH on Water Distribution in Man as Measured by Antipyrine, T 1824 and Bromide. Ziff, M., Simson, J., and Bunim, J. J.: J. Clin. Investigation **31**: 829, 1952.

Three patients with rheumatoid arthritis, 1 with rheumatic spondylitis, and 1 with rheumatic fever and polyarthritis were treated with ACTH (100 to 120 mg. per day for four weeks). The variations in plasma volume, extracellular fluid volume, and total body chloride were followed using T 1824 dye, antipyrine, and bromide space determinations before, during, and after ACTH administration. All patients showed retention of body water while under treatment. Two with obvious edema retained water predominantly in the extracellular space. In 2 other cases without evidence of edema, water was retained intracellularly. In 1 patient, an initial increase in bromide space indicated chloride retention which diminished later while total body water, measured by antipyrine, increased. Plasma volume, measured by T 1824 dye, rose in 3 patients and fell in 2. It is concluded that "the manner of water retention by different individuals in response to ACTH is variable." K.

Effect of Adrenocorticotropic Hormone (ACTH) on Serum Amylase Activity and Carbohydrate Metabolism. Tribby, C. L.: Am. J. Clin. Path. **22**: 855, 1952.

Serum amylase determinations were carried out immediately before and twenty-four hours after the intramuscular injection of ACTH (25 mg. followed four hours later by 15 mg.) in 20 patients with rheumatoid arthritis. Pretreatment amylase values, all within the normal range, averaged 81. Following the administration of ACTH, these values rose above the control values in 18 patients. Eight of these determinations were elevated above the normal range of amylase activity. The posttreatment average value was 138. Glu-

cose tolerance tests were normal initially. Twenty-four hours after treatment with ACTH, decreased tolerance was noted in 12 patients, normal tolerance in 6, and increased tolerance in 2 patients. K.

Inspiratory-Expiratory Vital Capacity Test of Pulmonary Function. Leslie, A.: Am. J. Med. **13**: 809, 1952.

A modified technique which provides a simple but accurate method for determining pulmonary function is presented. The test depends upon a comparison of the magnitude and contour of the inspiratory and expiratory vital capacity recordings. The former is the amount of air inhaled maximally after a complete exhalation; the latter is the amount exhaled maximally following completion of the inspiratory phase. It was shown that the expiratory vital capacity in 34 patients with pulmonary emphysema was less than the inspiratory vital capacity and that the kymographic curve produced by the expiratory phase was consistently slower than the inspiratory recording. Normal control subjects did not show these changes. In 15 patients suffering from pulmonary impairment of cardiac origin, the readings were similar to those found in the normal control group. Obese individuals gave readings of the same magnitude as those in pulmonary emphysema, but the slope of the expiratory curve was found to be uniformly normal. F.

Changes in Eosinophile Count of Mice With Venesections Repeated at Intervals of Several Days. Halberg, F.: Proc. Soc. Exper. Biol. & Med. **82**: 160, 1953.

The mean eosinophile count of inbred mice maintained in a standardized environment fell progressively in tail blood samples taken at four-day intervals. In one group, the mean initial count of 125/mm.^{3} fell after the fifth interval count on the sixteenth day to 72/mm.^{3} It is essential, therefore, to know the past history of animals which are to be used in experiments involving quantitative studies of eosinophiles. M. Cohen.

Studies in Cortisone.

II. Metabolism in Cortisone Poisoning; Effect of Cortisone on Tissue Culture of Fibroblasts. Alrich, E. M., Carter, J. P., and Lehman, E. P.: Surgery **32**: 326, 1952.

Cortisone was administered subcutaneously to rats in large doses, 30 to 40 mg. per kilogram of body weight, daily, for thirty-five days. After two days, there was loss of appetite and a negative balance of potassium, sodium, chloride, and nitrogen, as compared to a control group. Within four to sixteen days, there was temporary adaptation. This was manifested by a return of appetite and reversion to positive nitrogen, sodium, and chloride balance. However, potassium remained in negative balance. After twenty-two to twenty-six days, the animals again showed poor appetite, negative nitrogen and electrolyte balance, lost weight, and soon became emaciated. The earliest death occurred on the twenty-fifth day; all except one were dead by the forty-first day. Pathologically, there was marked atrophy of the adrenal cortex. The lungs showed extensive areas of pneumonia which apparently was a terminal event. The animals seemed to resist infection poorly.

Tissue cultures of rat striated and cardiac muscle were grown and various concentrations of cortisone were added to the nutrient solutions. Cortisone did not prevent growth of fibroblasts nor change the character of the cells, as had previously been reported. J. S.

Miscellaneous

Studies on the Generalized Shwartzman Reaction. I. General Observations Concerning the Phenomenon. Thomas, L., and Good, R. A.: J. Exper. Med. **96**: 605, 1952.

Meningococcal toxin was administered by ear vein to young rabbits and the lethal effect of a single dose of toxin was investigated in 265 animals: those receiving high concentrations became ill within one to two hours (dyspnea, weakness, arched necks, and sometimes clonic convulsions). Most of them recovered within twelve hours and remained well. After forty-eight hours, the animals were sacrificed and, with the exception of 2 rabbits which showed renal cortical necrosis, gross and histologic studies of the tissues were negative. In a series of over 200 rabbits given toxin intracutaneously none became ill or died.

In contrast, when 2 intravenous injections of the toxin were administered, most of the animals became weak and dyspneic within four to six hours. Diarrhea often developed after twelve hours and death usually occurred eighteen to twenty-four hours after injection. Petechiae were present in the ears a few hours before death. Animals dying within four hours of the second injection showed no gross pathologic changes. Animals which died after four hours or which were sacrificed at twenty-four hours showed bilateral cortical necrosis of the kidneys. The proportion of animals affected and the severity of the lesions was dependent upon the doses of toxin administered. Such reactions failed to occur when both 2 c.c. doses of toxin were diluted 1:320 or higher.

Lesions were found in organs other than the kidney and the more severe the renal lesion the more extensive and severe were the lesions in the lungs, heart, liver, spleen, thymus, lymph nodes, and gastrointestinal tract. In animals mildly affected, only renal lesions were present. The renal lesions were maximal twenty-four hours after the second injection and were associated with marked rise in blood nonprotein nitrogen. Animals sacrificed four hours after the second injection exhibited masses of eosinophilic homogeneous material in the glomerular capillary lumen. Chemical studies to date suggest that it is a mucopolysaccharide of "fibrinoid" type and the absence of abnormality of the capillary walls suggested that it was formed within the circulating blood, but not as a local product or constituent of the vessel walls. Kidneys removed between four and twenty-four hours after the provocative dose of toxin revealed tubular necrosis and hemorrhage into the parenchyma of the renal cortex and occlusion of glomerular capillaries. It is suggested that tubular necrosis may be primarily due to interference with glomerular capillary circulation by the eosinophilic plugs. In the heart, myofiber necrosis was discovered which was not related to the severity of renal lesions. Hemorrhagic and necrotic lesions were observed in other tissues. No eosinophilic "plugs" could be found in organs other than the kidney. The optimal preparative and provocative doses of meningococcal toxin were determined and it was found that when excessive amounts of toxin were used in preparation the reaction was inhibited. The optimal interval between the 2 doses varied from twelve to twenty-four hours. When the intervals were less than six hours or over four days, renal necrosis could not be produced. It was further determined that repeated injections of toxin at hourly intervals did not favor the development of renal necrosis, indicating that continual exposure to toxin was not an important factor. Cortisone administered to rabbits for three days prior to the injection of a single very large dose of toxin increased the mortality rate and only those animals treated in this manner developed renal

cortical necrosis. Cortisone and ACTH also enhanced the development of lesions in animals subjected to 2 intravenous injections of toxin. Pituitary somatotropic hormone administered in a dose of 10 mg. per kilogram per day for three days before the experiment neither affected the incidence of the Shwartzman reaction nor did it alter cortisone enhancement of this reaction. It was observed that circulating polymorphonuclear leukocytes dropped to 200 or less per cubic millimeter beginning thirty minutes after the initial injection of toxin and rose again four hours later to higher than pretreatment levels. When, twenty-four hours later, the provocative injection of toxin was made, the leukocytes dropped as before and began to rise again after four hours, "reaching extremely high levels by the end of the second day in some animals. The development of an extremely elevated polymorphonuclear leucocyte count after the second injection of toxin was found to be consistently associated with the occurrence of bilateral renal cortical necrosis." Nitrogen mustard administered intravenously to depress the count of polymorphonuclear leukocytes inhibited the Shwartzman phenomenon. When the bone marrow was protected by clamping the aorta for five minutes after the injection of nitrogen mustard, leukopenia did not occur and the Shwartzman phenomenon was not inhibited. The generalized Shwartzman reaction could not be elicited in toxin-prepared animals by nonbacterial materials, such as kaolin, starch, rabbit liver tissue, rabbit liver glycogen, or human serum (the latter in human-serum-sensitized rabbits). In this respect, the general Shwartzman phenomenon differs from the local phenomenon. K.

Relationship of Postcholecystectomy Disturbances to Bacterial Sensitivity. Jennings, W. K., Ortega, L. R., and Braslow, L.: Surg., Gynec. & Obst. **95**: 439, 1952.

Persistence of preoperative symptoms occurred in 28 per cent of a series of 148 patients following cholecystectomy. Among the patients with postcholecystectomy syndrome, 45 per cent had a definite clinical history of allergy. At operation, the bile was cultured; in the 30 per cent of cases in which positive cultures were obtained, a killed bacterial suspension was made from each culture for intracutaneous testing. Of 51 positive cultures, 18 showed streptococci, 9 showed staphylococci, and 24 were of the intestinal bacillary group.

Seventy-four per cent of the patients tested gave positive reactions to the bacteria isolated from their respective gall bladders. It is postulated that sensitivity to residual bacterial infection may explain those cases in which the cholecystic syndrome persists after cholecystectomy. Treatment with autogenous vaccine is suggested in such cases. J. S.

Eosinophilic Granuloma of the Lung. Lackey, R. W., Leaver, F. Y., and Farrinacci, C. J.: Radiology **59**: 504, 1952.

Two cases of eosinophilic granuloma of the lung and one case involving both lung and bone are presented. All three cases were confirmed by surgical biopsy and histologic study. The clinical manifestations were mild and the course benign with eventual recovery. Only one case showed an elevated blood eosinophilia. The differential diagnosis is discussed. Eosinophilic granuloma limited to the lung had not been reported previously. J. S.

Eosinopenia Induced by Emotional States. Dreyfuss, F., and Feldman, S.: **Acta med. Scandinav. 144**: 107, 1952.

Eosinophile counts were made on 31 medical students before they were given oral examinations on various subjects. Control counts were done

exactly twenty-four hours later. The pre-examination counts showed an average drop of 44 per cent. In a few students, the low eosinophile count persisted for several days and was attributed to continued tension. There was an average drop of 42 per cent in the preoperation eosinophile counts in 10 women admitted for diagnostic curettage.

The decrease in eosinophile counts in both groups is ascribed to emotional stress. Emotionally induced eosinopenia may interfere with the evaluation of eosinophile counts in various stress conditions or with the study of the effects of drugs and hormones. The extreme variability of "normal eosinophile counts" may, in part, be caused by this factor. H.

Periarteritis Nodosa in Children. Report on Two Cases. Ritama, V., and Lahdensun, S.: Ann. med. intern. fenn. **40**: 37, 1951.

Periarteritis nodosa was observed in a 17-month-old male child whose original illness seemed to be a mild attack of scarlet fever. The child had been vaccinated with BCG at birth and showed evidence of "vaccination TB" at autopsy. The authors believe that the streptococcal infection was the primary factor which induced the periarteritis.

The second case of periarteritis nodosa was seen in a 9-year-old girl whose presenting symptoms were headache and impaired vision. Death occurred fifteen months later. Extensive lesions of periarteritis nodosa were found at autopsy.

The literature on the occurrence of periarteritis in children is reviewed. H.

The Half Life of Homologous Gamma Globulin (Antibody) in Several Species. Dixon, F. J., Talmage, D. W., Maurer, P. H., and Deichmiller, M.: J. Exper. Med. **96**: 313, 1952.

Gamma globulins from human adult blood, human cord blood, and from bovine, rabbit, dog, mouse, rabbit, guinea pig, and monkey sera were labeled with I_{131}. Intravenous injections of 5 mg./kg. of the labeled globulin were administered to 14 adults, 11 children, and to the animals mentioned above, each species receiving homologous antibody. The half life of homologous antibody in the plasma varied with the species, the average time in days being for the mouse 1.9, guinea pig, 5.4, rabbit, 4.6 to 5.7 days, cattle, 21.2 days, monkey, 6.6, dog, 8.0, adult, 13.1, and child (6 months to 8 years of age), 20.3 days. The authors noted that the half life of globulin varied directly with the size of the species and was influenced by the metabolic rate. Ten rabbits, treated with thyroxin so that their oxygen consumption was double the normal rate, showed a decrease in antibody half life to 3.2 days. The longer half life of antibody in children as compared to that in adults could not be explained. The rates of antibody persistence found by this technique checked closely with those reported by other workers. K.